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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|---|---|---|---|
| 09/445,865 | 02/11/00 | BURKE | P ERD100 |

EXAMINER

HM22/0213

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| ART UNIT | PAPER NUMBER |
|---|---|
| 1642 | 7 |

DATE MAILED: 02/13/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

| Office Action Summary | Application No. 09/445,865 | Applicant(s) BURKE ET AL. | |
|---|---|---|---|
| | Examiner Gary B. Nickol Ph.D. | Art Unit 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If the period for reply specified above is less than thirty (30) days, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *04 May 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claims *1-40* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

15)☐ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☒ Other: *fax sheet* .

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## DETAILED ACTION

Claims **1-40** are pending in the application and are currently under prosecution.

**Please Note:** In an effort to enhance communication with our customers and reduce processing time, Group 1640 is running a Fax Response Pilot for Written Restriction Requirements. A dedicated Fax machine is in place to receive your responses. The Fax number is 703-308-4315. A Fax cover sheet is attached to this Office Action for your convenience. We encourage your participation in this Pilot program. If you have any questions or suggestions please contact Anthony Caputa, Ph.D., Supervisory Patent Examiner at 703-308-3995. Thank you in advance for allowing us to enhance our customer service. Please limit the use of this dedicated Fax number to responses to Written Restrictions.

### *Election/Restrictions*

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in response to this action, to elect a single invention to which the claims must be restricted.

Group 1, claim(s) 1-7,24, drawn to a protein compound comprising a target cell-specific portion and human NAD(P)H:quinone reductase 2.

Group 2, claim(s) 1-7,24, drawn to a polynucleotide encoding NQO2, variant, fragment, fusion, or derivative.

Group 3, claim(s) 8-12,24 drawn to a recombinant polynucleotide comprising a target cell-specific promoter operably linked to a polynucleotide encoding NQO2.

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Group ~~3~~ 4, claim(s) 13-17, drawn to a therapeutic system comprising a protein compound comprising a target cell-specific portion and human NAD(P)H:quinone reductase 2.

Group ~~4~~ 5, claim(s) 13-17, drawn to a therapeutic system comprising a polynucleotide encoding NQO2, variant, fragment, fusion, or derivative.

Group ~~5~~ 6, claim(s) 13-17, drawn to a therapeutic system comprising a recombinant polynucleotide comprising a target cell-specific promoter operably linked to a polynucleotide encoding NQO2.

Group ~~6~~ 7, claim(s) 18-23, drawn to a method of treating a patient with a target cell to be destroyed comprising administering a protein compound comprising a target cell-specific portion and human NAD(P)H:quinone reductase 2.

Group ~~7~~ 8, claim(s) 18-23, drawn to a method of treating a patient with a target cell to be destroyed comprising administering a polynucleotide encoding NQO2, variant, fragment, fusion, or derivative.

Group ~~8~~ 9, claim(s) 18-23, drawn to a method of treating a patient with a target cell to be destroyed comprising administering a recombinant polynucleotide comprising a target cell-specific promoter operably linked to a polynucleotide encoding NQO2.

Group ~~9~~ 10, claim(s) 25-28, drawn to a method of using a protein compound comprising a target cell-specific portion and human NAD(P)H:quinone reductase 2.

Group ~~10~~ 11, claim(s) 25-28, drawn to a method of using a polynucleotide encoding NQO2, variant, fragment, fusion, or derivative.

Group ~~11~~ 12, claim(s) 25-28, drawn to a method of using a recombinant polynucleotide comprising a target cell-specific promoter operably linked to a polynucleotide encoding NQO2.

Group ~~12~~ 13, claim(s) 29-33,40, drawn to a method of treating a human patient with a target cell to be destroyed wherein the target cell expresses NQO2

Group ~~13~~ 14, claim(s) 34-35, drawn to a therapeutic system comprising a prodrug and nicotinamide riboside.

Group ~~14~~ 15, claim(s) 36-37, drawn to a method of using a therapeutic system comprising a prodrug and nicotinamide riboside.

Group ~~15~~ 16, claim(s) 38, drawn to a method of using a prodrug in the manufacture of a medicament for treating a human patient.

Group ~~16~~ 17, claim(s) 39, drawn to a kit comprising a means for determining whether a target cell to be treated expresses NQO2 and NRH or an analogue thereof which can pass reducing equivalents to NQO2.

The inventions are distinct, each from the other because of the following reasons:

A national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept. Unity of invention is fulfilled only when there is a technical relationship among the inventions involving one or more of the same or corresponding special technical features which define a contribution over the prior art. If there is no special technical feature, if multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application will be considered as the main invention in the claims, see PCT article 17(3) (a) and 1.476 (c), 37 C.F.R. 1.475(d).

The inventions listed as Groups 1-16 do not relate to a single inventive concept under PCT Rule 13.1 because under PCT Rule 13.2 they lack the same or corresponding special technical features for the follow reasons;

The technical feature linking groups 1-16 appears to be a compound comprising a target cell-specific portion and human NQO2 or a variant or fragment or fusion or derivative which has substantially the same activity as NQO2 towards a given prodrug. By virtue of the International Search Authority in PCT/GB 98/01731, Knox et al. (Cancer and Metastasis Reviews, Vol. 12, No.2, 1993) teach such a compound comprising a target cell-specific portion and human NQO2 or a variant or fragment or fusion or derivative which has substantially the same activity as NQO2 towards a given prodrug (abstract, and pages 207-210, and Figure 10).

**Species**

Groups 1-2 (Claims 4- 5) are generic to a plurality of disclosed patentably distinct species comprising the following molecules:

a)an antibody or fragment or derivative

b)a macromolecule

The products of the above species represent separate and distinct molecules with different structures and functions such that one species could not be interchanged with the other. As such, each species would require different searches and the consideration of different patentability issues.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol, Ph.D.
Examiner
Art Unit 1642

GBN
February 9, 2001

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

SUSAN UNGAR, PH.D
PRIMARY EXAMINER